Achievement of a Suitable Basis of Comparison in Phase 2 and Phase 3 Pediatric Somavaratan Clinical Trials (VERTICAL, VISTA, and VELOCITY Studies) and for the Comparison of Somavaratan to Daily Recombinant Human Growth Hormone (rhGH)

Number: SAT 016
Category: Pediatric Endocrinology

Authors

Philippe Backeljauw MD (/tristar_endo17/speaker/9f6300891abea35983bbd25dff9beef8)

Body

Philippe Backeljauw[*1], Bradley Scott Miller[2], Nancy Wright[3], Aristides K Maniatis[4], Michael Stalvey[5], Eric Humphriss[6], R. William Charlton[6] and George M Bright[6]
[1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]University of Minnesota Masonic Children's Hospital, Minneapolis, MN, [3]Florida State University College of Medicine, Tallahassee, FL, [4]Rocky Mountain Pediatric Endocrinology, Centennial, CO, [5]University of Alabama at Birmingham, Birmingham, AL, [6]Versartis, Inc., Menlo Park, CA

The therapeutic potential of rhGH in pediatric GHD (PGHD) has been recognized for over three decades, but achievement of optimal efficacy outcomes (i.e., height velocity [HV]) not only depends on a number of variables such as age, body weight, HV, IGF-I SDS, skeletal maturation, and GH_{max}, at time of treatment initiation (1), but may be compromised when patients do not adhere to burdensome regimens of daily subcutaneous injections required for current formulations (2). Somavaratan is a novel long-acting rhGH fusion protein with $t_{1/2}$ > 100 hours, previously shown to improve HV and IGF-I in pre-pubertal children with GHD in a multi-center, randomized Phase 1b/2a study, VERTICAL (3, 4). Over 200 pre-pubertal GHD subjects have been enrolled in somavaratan clinical trials; 136 subjects are participating in a Phase 3 non-inferiority trial (VELOCITY) of somavaratan versus daily rhGH (NCT02339090). The primary efficacy endpoint of these trials is HV. An equable basis of comparison of efficacy outcomes requires that the distribution of clinical characteristics known to affect HV outcomes be similar between the somavaratan trials and between the somavaratan and daily rhGH arms of the non-inferiority trial. In our published Phase 1b/2a study of pre-pubertal GHD children (4), the primary determinants of first year HV included patient age at treatment onset and the severity of the GHD state. To achieve the valid basis of comparison, similar inclusion/exclusion criteria are used for all somavaratan trials. Further, a stratification procedure based on region, expected median age, and expected median baseline IGF-I SDS was employed for the randomization to daily rhGH or somavaratan. In the non-inferiority trial, a total of 104 patients were randomized to the somavaratan arm and 32 to the daily rhGH arm. For the somavaratan and daily rhGH arms of the Phase 3 non-inferiority trial, the baseline mean (± SD) ages were 7.07 ± 2.0 vs. 7.03 ± 2.4 years; mean maximal stimulated GH were 5.77 ± 2.6 vs 5.87 ± 2.5 ng/ml; mean height-SDS were -2.76 ± 0.7 vs -2.64 ± 0.7; mean IGF-I SDS were -1.72 ± 0.7 vs. -1.87 ± 0.9; and mean bone ages were 5.28 ± 1.9 vs. 5.29 ± 2.2 years. These numerical differences in mean values are not clinically

meaningful. For the Phase 2 somavaratan trial (n = 64), the mean age was 7.8 ± 2.4; meanheight-SDS was -2.6 ± 0.6; mean IGF-I SDS was -1.7 ± 0.8; and mean bone age was 6.4 ± 2.4. No clinically meaningful differences exist between the Phase 2 and Phase 3 somavaratan trials in PGHD. In conclusion, the use of consistent inclusion/exclusion criteria in the various phases of somavaratan clinical trials and the use of a stratification procedure to balance arms for clinical characteristics affecting the primary outcome measure in a non-inferiority trial has yielded similar treatment populations; thus, a valid basis of comparison between treatment populations has been achieved.

Disclosure: PB: Investigator, Versartis, Inc., Advisory Group Member, Versartis, Inc.. BSM: Advisory Group Member, Abbvie, Coinvestigator, BioMarin, Coinvestigator, Armagen, Principal Investigator, Alexion, Principal Investigator, Endo Pharmaceuticals, Ad Hoc Consultant, Ferring Pharmaceuticals, Principal Investigator, Genentech, Inc., Principal Investigator, Novo Nordisk, Ad Hoc Consultant, Novo Nordisk, Ad Hoc Consultant, Pfizer, Inc., Ad Hoc Consultant, Sandoz, Principal Investigator, Sandoz, Scientific Content Contributor, Up To Date, Principal Investigator, Versartis, Ad Hoc Consultant, Versartis, Coinvestigator, Shire, Principal Investigator, Tolmar, Coinvestigator, Eli Lilly & Company. NW: Investigator, Novo Nordisk, Investigator, Versartis, Inc.. AKM: Investigator, Versartis, Investigator, Ascendis, Investigator, OPKO, Investigator, Novo Nordisk, Principal Investigator, Alexion, Principal Investigator, Genentech, Inc.. MS: Advisory Group Member, Vertex Pharmaceuticals, Consultant, Versartis, Inc., Investigator, Versartis, Inc.. EH: Employee, Versartis, Inc., Employee, Versartis, Inc.. RWC: Employee, Versartis, Inc., Employee, Versartis, Inc.. GMB: Consultant, Versartis, Inc..

Please take note of the Endocrine Society's News Embargo Policy at: https://www.endocrine.org/news-room/endo-annual-meeting (https://www.endocrine.org/news-room/endo-annual-meeting)

Sessions

SAT 001-047 Pediatric Endocrinology: Growth, Puberty, Adrenal and Bone
Saturday, Apr 01 1:00 PM
OCCC - West Hall B (EXPO Hall)
(/tristar_endo17/event/9f6300891abea35983bbd25dff56d8c3)